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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HILL, MYRON G	

ART UNIT	PAPER NUMBER
1648	

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17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/668,154	GAUTVIK ET AL.	
	Examiner	Art Unit	
	Myron G. Hill	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *17* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 26 June 2003 has been entered.

Claim 21 is under consideration.

Drawings

The replacement drawings were received on 26 June 2003. These drawings are acceptable.

Rejections Maintained Withdrawn

Claim 21 was rejected under 35 U.S.C. 102(e) as being anticipated by Kronenberg et al. (US RE37919). Applicant has shown priority to a date earlier than the cited reference to the matter in the claims.

Rejections Maintained

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim is drawn to making an intact hPTH(1- 84) in yeast or E. coli that is reactive with antibodies against human PTH, has same molecular weight as human PTH, and migrates as a single band when run on a gel.

Applicant argues that a) the claims are drawn to intact hPTH, b) the recited invention is enabled by the specification, and c) the claimed invention is enabled for the use of E. coli in the recited process.

Applicant's arguments have been fully considered and found persuasive in part.

The rejection is modified to be a scope of enablement rejection.

a) The claims are drawn to intact hPTH.

b) Applicant's argument regarding enablement is not found persuasive. Example 8, encompassing page 34, lines 11- 17, as well as Figure 12 lane 2, clearly disclose two bands are present. The cited passages only teach expression in transfected yeast in which "[t]wo major bands were seen in the medium from the pSS alphaL X5-HPTH1 transformant that were not present in the medium from the p alphaL X5 transformant: one band approximately 9000 daltons, the expected size of hPTH, and one band of approximately 16000 daltons that could correspond to an unprocessed MFalpha1-HPTH fusion product [page 34, lines 11-17]." Figure 12, lane 2 clearly shows two bands. Claim 21 (c)

part (3) requires a product that "migrates as a single band when subjected to gel electrophoresis." The cited passages do not produce the product required by the claim.

Purification steps needed to enable the claimed invention are not in the claims or the specification. The specification teaches that degradation was a problem in the expression of hPTH(1- 84) and only up to 20% of the immunoreactive material secreted was intact hPTH(1- 84) [page 15, lines 26- 28]. The level of purification/ sample preparation required to subject a sample to gel electrophoresis is much less than the level of purification required when the protein is subject to degradation. The specification does not teach how to purify intact hPTH (1- 84) so that it runs as a single band when subjected to gel electrophoresis and is not degraded. Example 8 only analyzes the culture medium, it does not "purify" it.

The argument that the invention is enabled for E. coli is not persuasive. Applicant cites portions of the specification as follows: page 7, lines 36- 38. This section asserts that intact hPTH was expressed in yeast and E. coli as a secretory peptide. It is noted the rest of the sentence that those lines are contained in discloses development of downstream technology and the paragraph immediately before the lines pointed out by Applicant relates in large part to purification requirements. Page 4, lines 1- 8 disclose a particular structure that is required for use in E. coli (preproparathyroid). At line 10 of the amended version of the cited paragraph, it states "may cause production microorganisms ...to produce preproparathyroid hormone at an increased rate and in an

improved yield over prior art transformed microorganisms." "May cause" is speculation and preproparathyroid is not "intact hPTH (1- 84)."

Thus, it is concluded that the specification is enabled for the production of a fusion protein in yeast that is cleaved, secreted and runs as two bands when the culture medium is subjected to gel. The specification does not teach how to purify this product to run as one band.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear what the metes and bounds of "substantially pure" is. It is not clear what is purified, if the microorganism is expressing intact hPTH, then what does the purification impart? The claim is also rejected because it lacks a conclusion such as "wherein substantially pure hPTH is produced." The claim is also not clear because the preamble indicates that substantially pure recombinant protein is produced; however, the steps are directed towards purifying intact hPTH. Claim 21 is also rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps.

See MPEP § 2172.01. The omitted steps are: In part (b) of the claim it is not clear what structure is required to produce intact hPTH in the microorganism. The specification discloses that a fusion protein was used that contained a promoter, a Staph A sequence or a yeast mating factor to express the exogenous hPTH (1- 84) as a fusion protein and in part (c) of the claim, it is not clear what is required of "purifying" or if it is essential for the production of the product as claimed. Page 7, lines 36- 38 of the specification states that intact hPTH was expressed as a secretory peptide. It is noted the rest of the sentence that those lines are contained in discloses development of downstream purification technology and the paragraph immediately before the lines relates in large part to purification requirements.

Is what is produced and purified an isolated homogenous protein? Or is it an intact hPTH in the presence of other forms?

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 21 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2. 6- 8, and 11 of U.S. Patent No. 6146852. Although the conflicting claims are not identical, they are not patentably distinct from each other because The application claim to a method is written in open language (comprising): a genitically engineered microorganism (yeast or E. coli) that produces an intact, exogenous hPTH (1- 84) within the organism and purifying hPTH (1- 84). The claim recites physical properties of the product as well. The patent claims recite a genetically engineered yeast that secretes the hPTH (1- 84) product and purifies it.

The product is considered to be the same in both because they are both hPTH (1- 84). The level of purity and physical properties are considered to be the same because no standard of purity is defined that differentiates them.

Claim 21 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 33- 35 of copending Application No. 08/340,664. The earlier claims are drawn to a product by process that requires the same method as the instant claim of a method comprising a yeast or E. coli microorganism that expresses exogenous HPTH (1-84) and is then purified. It would be obvious to use the method of the product by process as a method to make hPTH (1- 84). Both products have the same

structure and both are purified so it would be expected that both would have the same physical properties.

This is a provisional obviousness-type double patenting rejection. It is noted that the prior application has just been released from appeal wherein the Board affirmed in part and reversed in part the Examiner. Neither the case or the decision are available to the Examiner of the instant application.

Conclusion

The claim is not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 703-308-4521. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4247. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Myron G. Hill
Patent Examiner
October 29, 2003

JEFFREY STUCKER
PRIMARY EXAMINER